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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/909,005	07/18/2001	Henry Yue	PF-0599-2 DIV	9313

27904 7590 12/02/2002

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/909,005	YUE ET AL.
	Examiner	Art Unit
	Maher M. Haddad	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 29-46* is/are pending in the application.

4a) Of the above claim(s) *29,32,34,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,30,31,33,35-42 and 46* is/are rejected.

7)☒ Claim(s) *45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 10/01/02 (Paper No. 9), is acknowledged.

2. Claims 10 and 29-46 are pending.

3. Claims 29, 32, 34, and 43-44 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 10, 30, 31, 33, 35-42 and 45-46 under consideration in the instant application.

4. This Office Action will be in response to applicant's arguments, filed 10/01/02 (Paper No. 9). The rejections of record can be found in the previous Office Action (Paper No.7).

5. Applicant's IDS, filed 7-18-01 (Paper No. 3), is acknowledged. However, the references were crossed out as the entire documents were not found. Applicant is invited to produce such documents. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

Applicants argue that it is mandatory for the Examiner to consider information previously considered in a parent application. The Examiner will consider the IDS once the documents are resubmitted.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 10, 30, 31, 33, 35-42 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which specifically binds to a polypeptide of SEQ ID NO:1 for a diagnostic assay, does not reasonably provide enablement for any antibody which specifically binds to any polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1 in claims 10 and 46. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' arguments, filed 10-01-02, Paper No. 9 have been fully considered but not persuasive, essentially for the reasons of record.

Applicants argue that the claim 10 recites not only that the variant polypeptides are at least 90% identical to SEQ ID NO:1, but also have "a naturally-occurring amino acid sequence." and the choice of amino acids to alter is made by nature. Contrary to Applicants' assertions, the specification fails to provide any naturally occurring amino acid sequence with 90% identity to SEQ ID NO:1 or defined the naturally occurring amino acid sequence at least 90% identical to the amino acid of SEQ ID NO:1. The specification on page 12, lines 10-18, provides only a 53 and overall 69% identity within the region from L25 to R204 of CJPDZ. Furthermore, CJPDZ contains a putative PDZ domain from R107 to T189 which shares 82% sequence identity with the PDZ domain of LIN-7. Furthermore, the specification on page 11, lines 16-23, defined a variant of CJPDZ polypeptide as an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes. ...More rarely, a variant may have "nonconservative" changes,... similar minor variations may also include amino acid deletions or insertions, or both.". The enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which 10% of the polypeptide would have been altered such that the resultant polypeptide would have retained the function of the starting polypeptide.

Applicants argue that the Colman *et al*, Abaza *et al*, Lederman *et al* and Li *et al* references are not relevant to the case at hand, since the mutations were "artificially" created in the laboratory and therefore, are not analogous to molecular evolution, which is profoundly influenced by natural selection. Furthermore, amino acid residues that are critical for protein function are conserved. Thus, the amino acid differences are likely to represent substitutions that do not alter protein function. Contrary to Applicants' assertions, Lederman *et al*, teach a correlation between the genetic structure and the phenotype of the encoded protein in relation to the binding of mAbs, for example a common African allele of CD4, which is considered to be a naturally occurring event, has been identified by non-reactivity with the monoclonal antibody, OKT4. Lederman *et al*, further teaches that an arginin→ tryptophan substitution at amino acid 240 relative to $CD4^{OKT+}$ is found in chimpanzee, rhesus macaque, mouse and rat CD4 suggesting that this mutation may confer unique functional properties to the $CD4^{OKT4-}$ protein. Therefore, Lederman *et al* demonstrated that even a single amino acid change can ablate binding of the monoclonal antibody. Furthermore, Colman *et al* teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Colman *et al* provide an example of escape mutants of viral antigens which were selected by growth of virus in the presence of monoclonal antibody (natural selection), provide many examples of the type of substitution which can render the antigen unrecognizable by the selection antibody.

Applicants argue that Ngo *et al* reference cited by the Examiner relating to structure-antigenicity relationships in proteins is simply not germane to whether one can make and use the polypeptide variants recited by the present claims regardless of the function of the SEQ ID NO:1 variants , one can make those polypeptide variants using the disclosure. Applicants further bring to the Examiner attention Brennet *et al* reference, wherein Brennet *et al* have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. Contrary to Applicant's assertions, the

specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1 is essential for maintain its functional activity and which changes can be made in the structure of SEQ ID NO: 1 and still maintained the same function.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention with the different antibodies as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

8. Claims 10, 30, 31, 33, 35-42 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments, filed 10-01-02, (Paper No. 9), have been fully considered but not found persuasive, essentially for reasons of record.

Applicants assert that the instant specification defined the claimed genus through the recitation of chemical structure of a CJPDZ protein of SEQ ID NO:1 and that instant claims do not define a genus which is "highly variant".

However, the Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, the CJPDZ protein and it's function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants, wherein the variant has at least 90% sequence identity of SEQ ID NO: 1.

9. Claim 45 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

10. No claim allowed

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
December 2, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
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